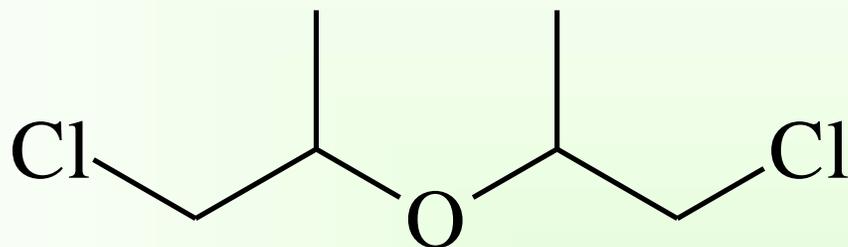
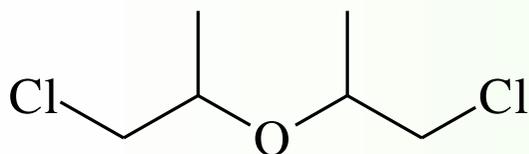


Technical Grade Bis(2-chloro-1-methylethyl) Ether

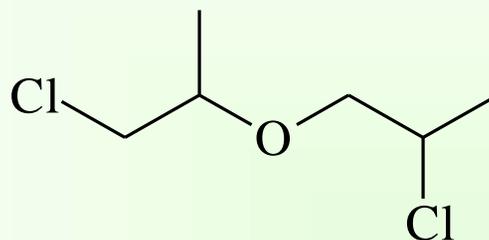


Molecular Weight: 171.07 CAS Registry No.: NA

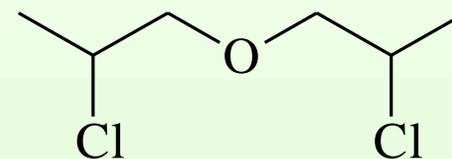
Technical Grade BCMEE



BCMEE



**2-Chloro-1-methylethyl
(2-chloropropyl) ether**



**Bis(2-chloro-*n*-propyl)
ether**

BCMEE Use/Occurrence

- By-product of propylene glycol and propylene oxide manufacture
- Solvent in paint and varnish removers, spotting agents
- Intermediate in dye synthesis
- Active ingredient in the nematocide Nemamorte[®] (Japan)

Carcinogenicity of BCMEE

- Carcinogenicity in humans:
 - No data
- Carcinogenicity in animals:
 - Oral gavage studies in mice (NTP, 1982)
 - Oral gavage studies in rats (NCI, 1979)
 - Dietary studies in mice (Mitsumori *et al.*, 1979)

Tumors in Male Mice (NTP, 1982)

Tumor Site and Type		Dose, mg/kg _{bw}		
		0	100	200
<i>Males</i>				
Lung: Alveolar/ Bronchiolar	Adenoma	5/50	13/50*	11/50
	Carcinoma	1/50	2/50	2/50
	Adenoma or carcinoma	6/50	15/50*	13/50
Liver	Adenoma	8/50	10/50	13/50
	Carcinoma	5/50	13/50*	17/50*
	Adenoma or carcinoma	13/50	23/50*	27/50*
	Metastases to lung	1/50	4/50	3/50
Stomach / Forestomach	Squamous-cell papilloma	0/49	1/50	1/50

* Significant increase above controls ($p < 0.05$ by Fisher Exact test).

Tumors in Female Mice (NTP, 1982)

Tumor Site and Type		Dose, mg/kg _{bw}		
		0	100	200
<i>Females</i>				
Lung:	Adenoma	1/50	4/50	8/50*
	Alveolar/ Bronchiolar	Carcinoma	0/50	0/50
	Adenoma or carcinoma	1/50	4/50	10/50*
Stomach / Forestomach	Squamous-cell papilloma	0/50	0/49	2/49
	Squamous-cell carcinoma	0/50	0/49	1/49

* Significant increase above controls ($p < 0.05$ by Fisher Exact test).

Non-positive Findings

- Rat oral gavage studies (NCI, 1979)
- Mouse dietary studies (Mitsumori *et al.*, 1979)

Genotoxicity of BCMEE

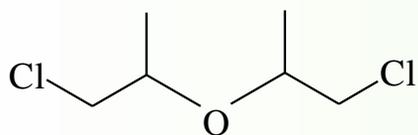
- Bacterial assays:
 - Mixed findings in *Salmonella* reverse mutation assays (with and without metabolic activation)
 - Non-positive findings in *Escherichia coli*

Genotoxicity of BCMEE (cont.)

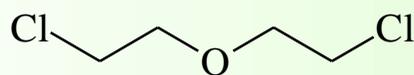
- Mammalian cell assays
 - Positive in mouse lymphoma forward mutation assay without metabolic activation
 - Positive for chromosomal aberrations (+S9) and SCE (+/-S9) in CHO cells
 - Positive for S-phase synthesis in mouse hepatocytes; Negative UDS

Structure-Activity Comparisons

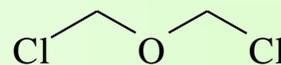
- Carcinogenicity of other haloethers:
 - bis(chloroethyl) ether (BCEE)
 - bis(chloromethyl) ether (BCME)
 - chloromethyl methyl ether (CMME)



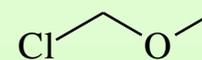
BCMEE



BCEE



BCME



CMME

BCMEE: Summary

- Animal evidence for carcinogenicity:
 - Induction of liver tumors in male mice
 - Induction of lung tumors in male and female mice
 - Some rare forestomach tumors in mice
- Other relevant evidence
 - Genotoxicity, structure-activity analogies